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(54) Abstract Title

Cosmetic composition for the improvement of hair growth

(57) A cosmetic method for the improvement of the growth of hair, whereby a composition containing botulinum toxin is administered to the scalp wherein the circulation of blood or supply of nutrients to the follicles, which are essential for hair growth, are disturbed, preferably by injection.

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Improving the growth of human head hair

The invention is concerned with improving the growth of human head hair and, inter alia, provides a cosmetic method for this purpose.

According to the current state of the art, substances (for internal and external application) and (mechanical and psychosomatic) methods are known, with the assistance of which the loss of head hair can be stopped or new growth stimulated.

A number of these substances contain anti-androgens which reduce the production of male hormones (androgens). Genes and hormones play the most significant part in so-called androgenetic hair loss.

This type of hair loss is preceded by changes or hardening in the connective tissue at the base of the hair. The hair is no longer held firmly or adequately nourished.

If a hair follicle with a predisposition to baldness is exposed to male hormones over a longer period of time, it produces fewer hairs.

Some anti-androgen substances cut off the access of androgens to the hair root. These are applied to the scalp. Other anti-androgen substances inhibit the transformation of testosterone (male sexual hormone) into dihydrotestosterone (DHT), which causes congenital baldness. These are taken orally.

The effectiveness of many of these substances is questionable and their side effects often lead to reductions in dosage. No account is taken of the fact that, with many of those affected, hair loss takes place

only in certain areas of the scalp.

According to state of the art, hair transplantations are also known, where existing healthy hair is transplanted to
5 areas of impaired hair growth in the same person.

Numerous patents are known whose purpose is the prevention of hair loss:

10 According to German patent no. 32 28 489 goat's milk butter, testes and placenta extracts have a slight but constant effect in counteracting hair loss.

The US patent application 994347 describes a treatment of
15 congenital baldness (alopecia).

The US patent 6 020 327 describes a treatment of hair loss where an aromatase inhibitor is administered.

20 The US patents 5 538 945 and 6 017 888 describe the stimulation of hair growth by a peptide-copper complex.

The US patent 5 861 142 describes a process for encouraging the keratinization of hair, nails and skin by
25 the therapeutic administration of benzimidazoles.

Many of the above substances and methods have also produced only very slight or questionable effect.

30 The aim of the invention is to describe a cosmetic method for improving the growth of human head hair which has a higher probability of success.

According to the present invention there is provided a
35 cosmetic method for improving the growth of human head hair as claimed in claim 1.

The cosmetic method according to the invention has a high probability of success, in particular for a selected group of persons.

5

According to the present invention there are also provided the uses, related to the cosmetic method, in accordance with claims 7 and 8.

10 According to the present invention there is further provided an injectable preparation, suitable for the cosmetic method, in accordance with claim 13. There is also provided a kit for making the injectable preparation.

15 The cosmetic method of the present invention makes use of the antispasmodic characteristics of botulinum toxin.

Botulinum toxin is a neurotoxin produced by the anaerobic bacterium *Clostridium Botulinum*.

20

There eight serologically distinct botulinum toxins, of which type A is the most widely studied.

25 The use of botulinum toxin for various purposes is known in the state of the art. However, the use of this toxin for improving the growth of human head hair is not known in the state of the art, and neither is such a use suggested in the state of the art.

30 In therapeutic applications, tiny quantities of botulinum toxin type A are injected directly into selected muscles to counteract involuntary contractions.

35 When botulinum toxin is injected into a muscle, certain nerve impulses are blocked, thereby reducing the tonus of the muscle in question. The full effect is achieved only

after a delay of several days. The therapeutic objective of local muscular relaxation with botulinum toxin is dependent on the individual symptoms and the requirements of the patient. The temporary muscular paralysis caused by botulinum toxin is temporary and reversible.

The following are the most common applications for botulinum toxin:

10 Treatment of

Eyelid spasm (idiopathic blepharospasm), hemifacial spasm (coexisting hemifacial dystonic movement), spasmodic torticollis (idiopathic rotating torticollis).

15

Equinovagis deformity.

In cosmetic medicine, botulinum toxin A is used, among other thing, for the treatment of forehead wrinkles and crow's feet.

20

Clinical studies suggest that it may also be useful in treating writer's cramp etc.

25 Botulinum toxin type A is most commonly available in dry solid form. Other constituents of the dry solid may be albumin human, lactose or sodium chloride. Before administering the injection, the dry solid is dissolved in a sterile physiological sodium chloride solution.

30

Specific indications for botulinum toxin are described in the following patents:

US patent 5,766,605 describes a method of treatment for autonomic nerve dysfunction with botulinum toxin.

35

US patent 5,714,468 describes a process for the reduction of migraine headache pain using botulinum toxin.

5 US patent 5 053 005 describes a non-surgical method of modulating spinal curvature in developing vertebrates using botulinum toxin.

10 US patent 4 932 936 describes a method and apparatus for pharmacological control of spastic urethral sphincters by injections of botulinum toxin A.

15 German patent DE 43 35 366 describes a process for manufacturing a crystalline botulinum toxin type A as a therapeutic medication for squints and blepharospasm.

US patent 5 721 216 describes an injectable therapy for control of muscle spasms and pain related to muscle spasms using botulinum toxin.

20 US patent 5 731 161 describes a botulinum toxin antibody-detection assay.

25 US patent 5 939 070 describes a hybrid botulinum neurotoxin.

In all the above applications of botulinum toxin, it is used primarily for the treatment of involuntary muscular spasms. Generally speaking the effects of botulinum toxin do not become noticeable until after about 3 - 4 days. The
30 duration of the therapeutic effect is between 3 and 10 months. A botulinum toxin treatment can be repeated indefinitely, however normally not until 10 weeks have expired.

35 However, as mentioned above, the use of botulinum toxin for improving the growth of human head hair is not known

in the state of the art, and neither is such a use suggested in the state of the art.

Under the scalp of the human head, the root of each individual hair is embedded in a pocket-shaped structure, the hair follicle. At the end of this hair follicle there are tiny capillary blood vessels which provide nourishment to the hair root. The skull is covered with a web of blood vessels resembling the branches of a tree. These supply the capillary blood vessels of the hair follicles with blood and nutrients. The skull is also covered by flat sinew and muscular cords.

Any disruption of the supply of blood and nutrients to the hair follicles can lead to hair loss, including normal daily hair loss, and hinder or inhibit hair growth such that the person concerned considers their hair growth to be cosmetically insufficient. Cosmetically insufficient hair growth in a certain group of people may also be attributable to a disruption in the supply of blood and nutrients to the hair follicles as a result of stress factors, including normal, everyday levels of stress.

It is known (e.g. from the source "Aroma Therapy for Common Ailments", Gaia Books, London 1991) that sporadic hair loss may be part of a reaction to severe stress or shock. "Stress in particular may lead to tension in the scalp, thereby preventing blood and nutrients from reaching the individual hair follicles. The starving hair roots then shrink in the follicle and the hairs drop out".

The group of persons whose typical reaction to stress - including normal day-to-day stress - involves cramps and/or tension in certain areas of the head (skin, muscles - e.g. by gritting teeth or clenching jaws) may particularly susceptible to cosmetically insufficient hair

growth. Among the parts of the head which may be affected are those which are essential for the growth of head hair, i.e. for the supply of blood and nutrients to the hair follicles.

5

It should be emphasized that these areas of the head include the scalp and hair as well as the muscles by which the circulation of blood on the scalp may be disrupted (e.g. though tension of the musculus temporalis with the
10 resulting reduction in the quantity of blood passing through this muscle to supply the hair follicles, or through the competing demand for blood and nutrients on the part of the permanently tensed muscle). The resulting loss of hair is most commonly seen in the front area of
15 the head and temples, causing the hairline to recede. This is due to the anatomical position of the blood vessels, muscles and sinews in the scalp.

Muscular tension as a reaction to stress tends to be much
20 more pronounced in men than in women, so that insufficient hair growth or hair loss occurs much more frequently in men than in women. Executives and businessmen are a group which is typically affected. In this group, insufficient hair growth or hair loss can be caused or be favoured from
25 the age of 20 onwards.

In order to reduce the tensions mentioned above and improve the growth of hair on the human scalp, according to the invention, a substance containing botulinum toxin
30 is administered to the areas of the head in which the circulation of blood, essential for the supply of nutrients to the hair follicles and consequent hair growth, is disturbed.

35 According to the invention, the substance is administered preferably by injection, which injection may be either

subcutaneous or intramuscular.

Botulinum toxin is available on the market. One example is "Botox", produced by the Allergan company.

5

Clostridium Botulinum toxin A (e.g. "Botox") is preferably sold as a dry powder substance. For use in an embodiment the present invention the Botulinum toxin powder is dissolved and diluted in an injection solution, for example a saline solution, e.g. an unpreserved, sterile physiological sodium chloride solution. Since Botulinum toxin can readily be denatured by physical agitation the dissolving and dilution of the powder in the solution should be carried out carefully. The required quantity of the resulting injectable preparation is drawn into a disposable hypodermic syringe of the appropriate size, having a fine needle.

In an embodiment of the present invention the quantity used may be, for example, 1.25 to 2.5 units of Botulinum toxin in 0.05 to 0.1 ml of injection (sodium chloride) solution for each injection point.

Muscular tension, in particular of the musculus temporalis, which runs across the scalp on both sides, can be measured more accurately by means of muscle tone measurements (electromyographic measurements, EMG). Such EMG measurement can be carried out immediately prior to treatment in accordance with the invention. The EMG measurement will show which muscles are overactive and to what degree. On the basis of the EMG measurement, the sites of administration of the substance can be precisely placed, thereby increasing the success of botulinum toxin therapy in promoting and improving the growth of hair.

35

Initially, a suitable dose is up to 50E in total for each

side of the head.

To optimize the absorption of the botulinum toxin by the contracted muscles and increase its paralytic effect,
5 these muscles should be massaged, or consciously tensed several times every 15 minutes for a period of two hours following the administration.

During the administration and for several hours
10 thereafter, the person should remain in an upright position. (After administration, the injected botulinum toxin diffuses into the tissue adjacent to the point of injection).

15 The effect of the treatment is manifest after 4 to 10 days, and may persist for from two months to more than six months. Thereafter, further treatment is needed. In subsequent treatments, dose can be increased slowly, if required, up to 100E.

20 It should be noted that the administration of botulinum toxin according to the invention should be carried out by trained and qualified persons, such as qualified medical staff or doctors working in the field of cosmetic
25 treatments.

The group of persons reacting to stress with muscular tension in the head area is easily defined. In many cases, tension of this kind is visible (formation of wrinkles),
30 tangible or detectable by EMG (electromyographic measurement).

With the group of persons concerned, it is occupational stress, including normal levels of occupational stress,
35 which manifests itself particularly through tension and consequent loss of hair in these areas of the head.

It is this group of persons at which the cosmetic method for improving hair growth according to the invention is primarily aimed.

5

Of all the botulinum toxins, it is type A whose effects have been most widely studied. It is therefore type A which is preferred for the cosmetic method according to the invention.

10

In the cosmetic methods according to the invention, the botulinum toxin may be injected in the same way as with previously known indications using a physiological sodium chloride solution as excipient.

15

The sustained success of the therapy is assured by repeating the cosmetic treatment at intervals of at least 10 weeks, or more usually, of several months.

C L A I M S

1. A cosmetic method for improving the growth of human head hair,
5 characterised by
administering a preparation containing botulinum toxin to those parts of the head in which the circulation of blood and/or supply of nutrients to the follicles which are essential for hair growth are disturbed.
- 10 2. A cosmetic method according to claim 1,
characterised by
said preparation comprising botulinum toxin and an injection solution, and administering said preparation by
15 subcutaneous or intramuscular injection.
3. A cosmetic method according to claim 1 or 2,
characterised by
said preparation containing botulinum toxin of type A.
- 20 4. A cosmetic method as claimed in claim 2, or claim 3
when read as dependent up claim 2, comprising injecting,
per injection point, 1.25 to 2.5 of botulinum toxin A in not more than 0.05 to 0.1 ml of the injection solution.
- 25 5. A cosmetic method according to claim 1, 2, 3 or 4,
characterised by the fact that
said preparation comprises sodium chloride solution as the injection solution.
- 30 6. A cosmetic method according to any of claims 1 to 5,
characterised by
repetition of administration of said preparation after 10 weeks at the earliest.
- 35 7. Use of botulinum toxin for the manufacture of a

preparation for a cosmetic treatment for improving the growth of human head hair, the cosmetic treatment comprising administering said preparation to those parts of the head in which the circulation of blood and/or supply of nutrients to the follicles which are essential for hair growth are disturbed.

8. Use of a preparation containing botulinum toxin for improving the growth of human head hair in a cosmetic treatment comprising administering said preparation to those parts of the head in which the circulation of blood and/or supply of nutrients to the follicles which are essential for hair growth are disturbed.

9. Use as claimed in claim 7 or 8, characterised in that the botulinum toxin is of type A.

10. Use as claimed in claim 7, 8 or 9, characterised in that said preparation is an injectable preparation comprising botulinum toxin and an injection solution.

11. Use as claimed in claim 10, wherein said preparation contains 1.25 to 2.5 units of botulinum toxin per each 0.05 ml to 0.1 ml of the injection solution.

12. Use as claimed in claim 10 or 11, characterised in that said injection solution is sodium chloride solution.

13. An injectable preparation comprising botulinum toxin and an injection solution, suitable for cosmetic treatment for improving the growth of human head hair, the cosmetic treatment comprising injecting said preparation into those parts of the head in which the circulation of blood and/or supply of nutrients to the follicles which are essential for hair growth are disturbed.

14. An injectable preparation as claimed in claim 13, characterised in that the botulinum toxin is of type A.

5 15. An injectable preparation as claimed in claim 13 or 14, characterised in that the preparation contains 1.25 to 2.5 units of botulinum toxin per each 0.05 ml to 0.1 ml of the injection solution.

10 16. An injectable preparation as claimed in claim 13, 14 or 15, characterised in that the injection solution is sodium chloride solution.

15 17. A kit for use in making and administering an injectable preparation as claimed in any of claims 13 to 16, the kit comprising a quantity of botulinum toxin in dry powder form, a quantity of unpreserved, sterile injection solution, a filling vessel for dissolving the dry powder toxin in the injection solution to form the
20 injectable preparation, and one or more disposable syringes for injecting the preparation.



INVESTOR IN PEOPLE

Application No: GB 0121161.4
Claims searched: 1-17

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Examiner: Dr William Thomson
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Patents Act 1977 Search Report under Section 17

Databases searched:

UK Patent Office collections, including GB, EP, WO & US patent specifications, in:

UK Cl (Ed.T): A5B (BFC)

Int Cl (Ed.7): A61K 7/06

Other: ONLINE: CAS-ONLINE, EPODOC, JAPIO & WPI

Documents considered to be relevant:

Category	Identity of document and relevant passage	Relevant to claims
X, E	WO 00/62746A1 (SCHWARTZ & FREUND) See whole document, in particular page 7, line 18 - page 8 line 4 and claims 1-12	1-16 at least

X	Document indicating lack of novelty or inventive step	A	Document indicating technological background and/or state of the art.
Y	Document indicating lack of inventive step if combined with one or more other documents of same category.	P	Document published on or after the declared priority date but before the filing date of this invention.
&	Member of the same patent family	E	Patent document published on or after, but with priority date earlier than, the filing date of this application.